UNITED STATES ENVIRONMENTAL PROTECTION AGENCY WASHINGTON, D.C. 20460



May 14, 2013

MEMORANDUM

SUBJECT: Acute Toxicity Review for EPA File Symbol: 10324-EEN

Product Name: Maguat CA-6

DP Barcode: 408869

FROM: Earl Goad, Biologist

Chemistry and Toxicology Team

Product Science Branch

Antimicrobials Division (7510P)

THRU: Karen Hicks, Team Leader

Chemistry and Toxicology Team

Product Science Branch

Antimicrobials Division (7510P)

TO: Jacqueline Hardy PM#35/Tom Luminello

Regulatory Management Branch II Antimicrobials Division (7510P)

Applicant: Mason Chemical Co.

PRODUCT FORMULATION FROM LABEL:

 PC Codes
 Active Ingredient(s):
 % by wt.

 021801
 Citric Acid.
 6.0

 Other Ingredient(s):
 94.0

Total: 100.00

I) BACKGROUND:

Technical Sciences Group Inc. on behalf of Mason Chemical Company has submitted a-pesticide application package for a new end use product EPA File Symbol: 10324-EEN "Maquat CA-6". This aqueous based product is described for household, institutional, and Industrial use as a bathroom cleaner, disinfectant and sanitizer.

The following documents were to support the Acute Toxicity data requirements for registration of their product.

- 1. Cover and Transmittal letter dated January 10, 2013.
- 2. Product Label undated.
- 3. Basic and three alternate Confidential Statements of Formula dated January 7, 2013. The formulations vary in composition relative to absence or presents of dyes and or formulations.
- 4. Six Acute Toxicity (six pack) studies and one test material characterization study. Studies received January 10, 2013.

<u>MRID</u>	Citation
49016403	Kukulinski, M. (2012) Acute Oral Toxicty Study in Rats with Maquat CA-6: Final Report. Project Number: 12/080/3/OCR. Unpublished study prepared by Tox Monitor Laboratories, Inc. 22p.
49016404	Kukulinski, M. (2012) Acute Dermal Toxicity Study of Maquat CA-6: (Rabbits): Final Report. Project Number: 12/080/4/OCR. Unpublished study prepared by Tox Monitor Laboratories, Inc. 21p.
49016405	Kukulinski, M. (2012) Acute Inhalation Toxicity Study in Rats with Maquat CA-6: Final Report. Project Number: 12/080/6/OCR. Unpublished study prepared by Tox Monitor Laboratories, Inc. 29p.
49016406	Kukulinski, M. (2012) Acute Eye Irritation Study in Rabbits with Maquat CA-6: Final Report. Project Number: 12/080/1/OCR. Unpublished study prepared by Tox Monitor Laboratories, Inc. 25p.
49016407	Kukulinski, M. (2012) Acute Dermal Irritation Study in Rabbits with Maquat CA-6: Final Report. Project Number: 12/080/2/OCR. Unpublished study prepared by Tox Monitor Laboratories, Inc. 19p.
49016408	Kukulinski, M. (2012) Skin Sensitization Study of Maquat CA-6: (Guinea Pigs): Final Report. Project Number: 12/080/5/OCR. Unpublished study prepared by Tox Monitor Laboratories, Inc. 26p.
49016409	Sinning, D. (2012) Maquat CA-6 Characterization Assays: Final Report. Project Number: 410/436/OCR. Unpublished study prepared by Case Consulting Laboratories, Inc. 7p.

II) FINDINGS:

- A. The test material is defined in all studies as being Maquat CA-6 Lot No. CM20120313-01. Chemical analysis was performed on this specific lot and it was found that the concentration of citric acid was within the recorded certified limits. This study is found to be acceptable.
- B. Acute Oral toxicity LD₅₀ was greater than limit dose of 5000 mg/kg by the Up and Down Procedure for female rats, resulting in a Category IV. This study is found to be acceptable.
- C. Acute Dermal toxicity LD₅₀ was greater than limit dose of 5000 mg/kg for both male and female rabbits, resulting in a Category IV. This study is found to be acceptable.
- D. Acute Inhalation toxicity (nose only) LC_{50} was greater than a dose of 2.6 mg/L for both male and female rats, resulting in a Category IV. This study is found to be acceptable.
- E. Primary Eye Irritation in rabbits minimal eye irritation was observed, all irritation cleared by 72 hours, Category III. This study is found to be acceptable.
- F. Primary Dermal Irritation in rabbits, no irritation was observed in any of three test animals resulting in Category IV. This study is found to be acceptable.
- G. Dermal Sensitization by Beuhler Technique Guinea Pig Sensitization, test material was found to be a non-sensitizer. This study is found to be acceptable.

III) The acute toxicity profile for EPA File Symbol: 10324-EEN "Maquat CA-6" is currently:

Study	MRID Number	Toxicity Category	Status
Acute Oral Toxicity	49016403	IV	Acceptable
Acute Dermal Toxicity	49016404	IV	Acceptable
Acute Inhalation Toxicity	49016405	IV	Acceptable
Primary Eye Irritation	49016406	III	Acceptable
Primary Skin Irritation	49016407	IV	Acceptable
Dermal Sensitization	49016408	Non- Sensitizer	Acceptable

IV) LABELING:

Keep Out of Reach of Children

- A. The signal word for EPA File Symbol 10324-EEN "Maquat CA-6" based on the category III for Eye Irritation is CAUTION.
- B. Precautionary labeling:

Hazards to Humans and Domestic Animals:

Causes moderate eye irritation. Avoid contact with eyes or clothing. Wear protective eyewear. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. Wear: Long-sleeved shirt and long pants, Socks, Shoes, and gloves.

C. First Aid:

If in eyes:

- -Hold eye open and rinse slowly and gently with water for 15-20 minutes.
- -Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
- -Call a poison control center or doctor for treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

Label Created in Lotus Notes Label Review System by: Earl Goad on 05/09/2013

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (OCSPP 870.1100) (UP AND DOWN PROCEDURE)

Product Manager: 34 Reviewer: Earl Goad(CTT)

MRID No.: 49016403 Completion Date: September 26, 2012

Study No.: 12-080-3

Testing Laboratory: Tox Monitor Laboratories, Inc.

Author: Michael Kukulinski, B.S., L.A.T.G

Quality Assurance (40 CFR §160.12): A Quality Assurance (QA) statement was included. A statement of Good Laboratory Practice (GLP) compliance was included stating that this study meets the requirements of 40 CFR Part 160: U.S. EPA (FIFRA).

Test Material: Maguat CA-6

Lot No. CM30120313-01

Clear Liquid

Dosage: Limit Test: 5,000 mg/kg (administered as received)

Species: Albino Rat; Sprague-Dawley

Sex: 10 Females. Females were nulliparous and non-pregnant.

Age: Young adult (9-11 weeks)

Weight: Day 0 (fasted) 219-230 grams at experimental start Source: Harlan Sprague Dawley, Indianapolis, Indiana.

Housing: Temperature Range: 66-77°F

Humidity Range: 30-70%

Photoperiod: 12-hour light/dark cycle

Acclimation: Quarantined 5 days

Conclusion:

1. Acute Oral LD₅₀ (mg/kg): Female Rats: Greater than 5,000 mg/kg

2. Toxicity Category: IV Classification: Acceptable

Procedure (Deviations from 870.1100):

No procedural deviations were reported or found.

Results:

Limit Test

Dosing Sequence	Animal No.	Dose Level (mg/kg)	Outcome	Time of Death	Gross Necropsy findings
1	390	5,000	S	Day 14-	No observable abnormalities
2	391	5,000	S	Day 14-	No observable abnormalities
3	392	5,000	S	Day 14-	No observable abnormalities

S – Survival; D – Death, For survivors, time of death at Day 14 means at terminal sacrifice.

Observations:

Body Weights

Animals survived the study. Study was terminated at 14 days. All test subjects exhibited weekly weight gains

Inlife Clinical Observations

All animals were active and health through the duration of the study.

Gross Necropsy Findings:

Individual gross necropsy findings both for external and internal organs and tissues in the thoracic and abdominal cavities no abnormalities were observed.

Statistical Analysis of the results

Based on AOT425 (Version 1.0) Test Results and Recommendations for Acute Oral Toxicity (OECD Test Guideline) Statistical Program.

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (OCSPP 870.1200)

Reviewer: Earl Goad(CTT) Product Manager: 34 Completion Date: September 27, 2012 MRID No.: 49016404

Study No.: 12-080-4

Testing Laboratory: Tox Monitor Laboratories, Inc.

Author: Michael Kukulinski, B.S., L.A.T.G

Quality Assurance (40 CFR §160.12): A Quality Assurance (QA) statement was included. A statement of Good Laboratory Practice (GLP) compliance was included stating that this study meets the requirements of 40 CFR Part 160: U.S. EPA (FIFRA).

Test Material Maguat CA-6

Lot No. CM30120313-01

Clear Liquid

Limit Test: 5,000 mg/kg (administered as received) Dosage:

Species: Zealand Albino Rabbils2

Sex: 5 Male and 5 Females. Females were nulliparous and non-pregnant.

Age: Young adult (at least 12 weeks old) 2.02 - 2.54 kg at experimental start Weight:

Source: Kuiper Rabbitry, Gary, Indiana Temperature Range: 63-73°F Housing:

Humidity Range: 30-70%

Photoperiod: 12-hour light/dark cycle

Acclimation: Quarantined 5 days

Conclusion:

1. **Demai LD**₅₀ (mg/kg): Greater than 5,000 mg/kg for

Male and Female Rabbits

2. Toxicity Category: IV Classification: Acceptable

Procedure (Deviations from 870.1100): No procedural deviations were reported or found

Results:

Reported Mortality

Dose Level	Number Dead / Number Tested				
(mg/kg)	Males	Females	Total		
5,050	0/5	0/5	0 / 10		

Observations:

All animals survived, gained body weight, and appeared active and healthy during the study. There were no signs of gross toxicity. However dermal irritation (erythema and edema) were observed for all animals on day 1 and erythema was observed for 7 of 10 test animals on day 2.

Gross Necropsy Findings:

No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the 14-day observation period.

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (OPPTS 870.1300)

(4 hour Whole Body Method)

Product Manager: 34 MRID No.: 49016405 Reviewer: Earl Goad(CTT)

Completion Date: October 12, 2012

Study No.: 12-080-6

Testing Laboratory: Tox Monitor Laboratories, Inc.

Author: Michael Kukulinski, B.S., L.A.T.G

Quality Assurance (40 CFR §160.12): A Quality Assurance (QA) statement was included. A statement of Good Laboratory Practice (GLP) compliance was included stating that this study meets the requirements of 40 CFR Part 160: U.S. EPA (FIFRA).

Test Material:

Maquat CA-6

Lot No. CM30120313-01

Clear Liquid

Dosage:

Aerosol of test substance neat. Albino Rat; Sprague-Dawley

Species: Sex:

5 Males, 5 Females. (Females were nulliparous and non-pregnant.)

Age:

Young adult (8 to 12) at start of study.

Weight:

Males & Females: 228-253 g at experimental start. Harlan Sprague Dawley, Indianapolis Indiana.

Source: Housing:

Temperature Range: 19-25°C

Humidity Range:

30-70%

Photoperiod:

12-hour light/dark cycle

Acclimation: Quarantined 5 days

Summary:

1) Acute Inhalation LC₅₀ (mg/L): Male and Female Rats: > 2.6 mg/L

2) Average MMAD: 3.57 µm at the 2.6 mg/L exposure level

3.) Toxicity Category: IV

Classification: Acceptable

Concentration:

	Group	Gravimetric Exposure Concentration (mg/L)	Nominal Concentration (mg/L)
ı	I	2.6*	27.4

^{*2.6} mg/L average concentration

Procedure (Deviations from 870.1300):

The laboratory reported that there were no deviations from their protocol.

Results:

Reported Mortality

Exposure	Nun	sted	
Concentration (mg/L)	Males	Females	Combined
2.6	0/5	0/5	0 / 10

Chamber Atmosphere

Exp. Conc.	Sample Time	MMAD	GSD	C	umul	ative 9	% of P Dian	article neter (fective	e Cuto	ff
(mg/L)	minutes	(µm)	(µm)	0.4	0.7	1.1	2.1	3.3	4.7	5.8	9	10
2.6	100	3.6	2.9	6.8	14.6	28.3	43.0	53.5	65.5	80.8	87.2	100
	200	3.6	2.7	4.9	14.3	28.1	44.9	54.3	66.6	83.4	88.5	100

¹Percent of particles smaller than corresponding effective cutoff diameter.

Chamber Environment During Exposure

	<u> </u>			
Exposure Level (mg/L)	2.6			
Chamber Volume (L)	400			
Average Total Airflow (Lpm) ¹	92			
Number of Air Changes Per Hour	12			
Mean Oxygen Content (%)	Not reported			
Mean Temperature (°F)	69			
Mean Relative Humidity (%)	95			

¹Total air = compressed air + diluent air

Clinical Observations: (2.6 mg/L exposure)

Males: and Females:

Appeared normal and each observation.

Gross Necropsy Findings: (2.6 mg/L exposure)

At terminal sacrifice on day 14 no observable external or internal (including thoracic and abdominal cavities) abnormalities were reported for any animal.

DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (OPPTS 870.2400)

(DRAIZE METHOD)

Product Manager: 34 MRID No.: 49016406

Reviewer: Earl Goad (CTT)
Completion Date: October 2, 2012

Study No.: 12-080-1

Testing Laboratory: Tox Monitor Laboratories, Inc.

Author: Michael Kukulinski, B.S., L.A.T.G

Quality Assurance (40 CFR §160.12): A Quality Assurance (QA) statement was included. A statement of Good Laboratory Practice (GLP) compliance was included stating that this study meets the requirements of 40 CFR Part 160: U.S. EPA (FIFRA).

Test Material:

Maguat CA-6

Lot No. CM30120313-01

Clear Liquid

Dosage:

0.1 mL administered as received

Species:

New Zealand White Rabbits

Sex:

3 Males

Age:

Young adult (10 to 12 weeks old) 2.45 to 2.68 kg at experimental start

Weight: Source:

2.45 to 2.68 kg at experimental sta Kuiper Rabbitry, Gary, Indiana

Housing:

Temperature Range: 63-73°F

Humidity Range:

30-70%

Photoperiod:

12-hour light/dark cycle

Acclimation: Quarantined 5 days

Summary:

1. Toxicity Category: III (minimal eye irritation clearing by 72 hours)

Classification: Acceptable

Procedure (Deviations from 870.2400): T

The laboratory didn't report any protocol deviations

Results:

The results of the study are displayed in the following summary tables.

. Severity of Irritation

Time Post Instillation	Rabbit 354-M	Rabbit 355-M	Rabbit 356-M	Mean Score
1 hour	8	6	8	7.3
24 hours	2	6	4	4.0
48 hours	0	0	2	0.7
72 hours	0	0	0	0

.Incidence of Irritation

Time Post	No. of Animals Testing "Positive" / No. of Animals Tes					
Instillation	Corneal Opacity	Iritis	Conjunctivitis			
1 hour	0/3	0/3	3/3			
24 hours	0/3	0/3	3/3			
48 hours	0/3	0/3	1/3			
72 hours	0/3	0/3	0/3			

Individual Scores for Ocular Irritation

Individual Scores for Ocular Irritation				
	Rabbit I	lo. 3 <mark>54(M</mark> ale)	
Observations		Hours Aft	er Treatmen	t
	1	24	48	72
I. Corneal Opacity	-	0	0	0
II. Iris	0	0	0	0
III. Conjunctivae				
A. Redness	1	11	0	0
B. Chemosis	1	0	0	0
C. Discharge	2	0	0	0
	Rabbit I	No. 355 (Male)	
Observations		Hours Aft	er Treatmen	t
	1	24	48	72
I. Corneal Opacity	-	0	0	0
II. Iris	0	0	0	0
III. Conjunctivae				
A. Redness	1	1	0	0
B. Chemosis	1	1	0	0
C. Discharge	1	1	0	2
,	Rabbit N	No. 356(Male)	
Observations		Hours Aft	er Treatmen	t
	1	24	48	72
I. Corneal Opacity	_	0	0	0
II. Iris	0	0	0	0
III. Conjunctivae		•		
A. Redness	1	1	1	0
B. Chemosis	1	0	0	0
C. Discharge	2	1	0	3

DATA REVIEW FOR ACUTE DERMAL IRRITATION TESTING (OPPTS 870.2500)

Product Manager: 34 Reviewer: Earl Goad (CTT)
MRID No.: 49016407 Completion Date: October 2, 2012

Study No.: 12-080-2

Testing Laboratory: Tox Monitor Laboratories, Inc.

Author: Michael Kukulinski, B.S., L.A.T.G

Quality Assurance (40 CFR §160.12): A Quality Assurance (QA) statement was included. A statement of Good Laboratory Practice (GLP) compliance was included stating that this study meets the requirements of 40 CFR Part 160: U.S. EPA (FIFRA).

Test Material: Maquat CA-6

Lot No. CM30120313-01

Clear Liquid

Dosage:

0.5 mL administered as received

Species: New Zealand White Rabbits

Sex:

3 Males

Age:

Young adult (10 to 12 weeks old) 2.77-2.89 kg at experimental start

Weight: Source: Housing:

Kuiper Rabbitry, Gary, Indiana <u>Temperature Range</u>: 17-23°C

Humidity Range:

30-70%

Photoperiod:

12-hour light/dark cycle

Acclimation: Quarantined 5 days

Summary:

1. Toxicity Category: IV (no skin irritation reactions found)

2. Classification: Acceptable

Procedure (Deviations from 870.2500): No procedural deviations were recorded or found.

Results: All animals were observed at 0.5, 24, 48, and 72 hours with irritation scores of 0 at any observation.

Incidence of Irritation

Time after Patch Removal	Erythema	Edema
30 minutes	0/3	0/3
24 hours	0/3	0/3
48 hours	0/3	0/3
72 hours	0/3	0/3

DATA REVIEW FOR SKIN SENSITIZATION TESTING (OPPTS 870.2600)

(BUEHLER METHOD)

Product Manager: 34 Reviewer: Earl Goad(CTT)
MRID No.: 49016408 Completion Date: October 9, 2112

Study No.: 12-080-5

Testing Laboratory: Tox Monitor Laboratories, Inc.

Author: Michael Kukulinski, B.S., L.A.T.G

Quality Assurance (40 CFR §160.12): A Quality Assurance (QA) statement was included. A statement of Good Laboratory Practice (GLP) compliance was included stating that this study meets the requirements of 40 CFR Part 160: U.S. EPA (FIFRA).

Positive Control Material: 1-Chloro-2,4-Dinitrobenzene

(Historical positive control test completed on April 5, 2012)

Test Material: Maguat CA-6

Lot No. CM30120313-01

Clear Liquid

Dosage: 0.4 mL administered as received based on low irritation potential found on

screen

Species: Hartley Guinea Pigs

Sex: Males -Total 32 animals (20 test, 10 neg. controls, and 2 pilot animals)

Age: Young adult (10 to 12 weeks old)
Weight: 316-490 grams at experimental start

Source: Kuiper Rabbitry, Gary, Indiana
Housing: Temperature Range: 63-73°F
Humidity Range: 30-70%

Photoperiod: 12-hour light/dark cycle

Acclimation: Quarantined 5 days

Method: Buehler Method

Summary:

1. Based on no incidence of skin sensitization having been elicited for Maquat CA-6 dosed at 100% concentration induction and challenge phase in male guinea pigs, this test material is found not to be a dermal sensitizer

2. Classification: Acceptable

Procedure Deviations from 870.2600: No deviations were reported.

Procedure:

Preliminary Irritation Testing: A group of animals was used to determine the highest non-irritating concentration (HNIC) of the test substance prior to the challenge dose. The fur was removed by clipping the dorsal area and flanks of each guinea pig. This area was divided into four test sites (two sites on each side of the midline) on each animal. The test substance was applied neat (100%) and also diluted with distilled water to yield w/w concentrations of 75%, 50%, and 25%, . Each concentration was applied (0.4 mL) to a test site using an occlusive 25 mm Hill Top Chamber. The sites were wrapped with Micropore then Kendall adhesive tape. After 6 hours of exposure, the chambers were removed and the test sites were gently cleansed of any residual test substance. Approximately 24 hours after application, each site was evaluated for local reactions (erythema) according to a scoring system provided in the laboratory report. From these results, the HNIC selected for the induction and challenge phase was a 100% concentration of test substance.

<u>Preparation and Selection of Animals</u>: On the day before initiation, the fur of a group of animals was removed by clipping the dorsal area and flanks. After clipping and prior to initiation, the animals were weighed and the skin was checked for any abnormalities. Only healthy animals without pre-existing skin irritation were selected for test. Animals were re-clipped prior to each dose.

Induction Phase: Once each week for three weeks, four-tenths of a milliliter of the undiluted test substance was applied. As above and approximately 24 and 48 hours after each induction application, readings were made of local reactions (erythema) according to the scoring system.

Challenge Phase: Twenty-seven days after the first induction dose, four tenths of a milliliter of a 100% of the test substance was applied to a naïve site on the right side of each animal as a challenge dose, using the procedures described above. These sites were evaluated for a sensitization response (erythema) approximately 24 and 48 hours after the challenge application according to the scoring system. In addition to the test animals, 10 guinea pigs from the same shipment were maintained under identical environmental conditions and were treated with the HNIC of the test substance at challenge only. These animals constituted the "naïve control" group.

<u>Historical Positive Control</u>: The procedures used in this study were validated using 1-Chloro-2,4-Dinitrobenzene. Historical positive control test completed on: April 5, 2012.

Results:

Induction Phase:

Test Animals (100% of undiluted test substance): Very faint to faint erythema (0.5) was noted 5 animals but only at 24 hours. Challenge Phase:

Test Animals (100% of the test substance): One of twenty test animals exhibited signs (very faint erythema [0.5]) 24 hours after challenge. Naïve Control Animals (100% of the test substance): No irritation was noted on any naïve control sites 24 or 48 hours after challenge.

Sensitization Response Indices (Erythema)

	Incidence d Resp		Severity ²	
	Hours		Hours	
	24	48	24	48
Test Animals – Challenge	1 / 20	0/20	0.025	0.0
Naïve Control Animals – Challenge	1/6	0 / 9 ²	0.08	0.0

Test Animal Group Skin Reaction Scores

Test Animal Group Skin Reaction Scores											
Treatment	Induction						Challenge				
Phase	1		2 ¹		3 ¹						
Concentration	100%		100%		100%		100%				
Hours ²	24 ³	48 ³	24 ³	48 ³	24 ³	48 ³	24	48			
Animal No. / Sex											
Test Group											
365 / M	0	0	0	0	0	0	0	0			
366 / M	0	0	0	0	0	0	0	0			
367 / M	0	0	0	0	0	0	0	0			
368 / M	0	0	0.5	0	0	0	0	0			
369 / M	0	0	0	0	0	0	0	0			
370 / M	0	0	0	0	0.5	0	0	0			
371 / M	0	0	0	0	0	0	0	0			
372 / M	0	0	0	0	0	0	0	0			
373 / M	0.5	0	0	0	0	0	0.5	0			
374 / M	0	0	0	0	0	0	0	0			
375 / M	0	0	0	0	0	0	0	0			
376 / M	0	0	0	0	0	0	0	0			
377 / M	0	0	0	0	0	0	0	0			
378 / M	0	0	0	0	0	0	0	0			
379 / M	0.5	0	0	0	0.5	0	0	0			
380 / M	0	0	0	0	0	0	0	0			
381 / M	0.5	0	0	0	0	0	0	0			
382 / M	0	0	0	0	0	0	0	0			
383 / M	0	0	0	0	0	0	0	0			
384 / M	0	0	0	0	0	0	0	0			
Naïve Control Group											
385 / M							0	0			
386 / M							0	0			
387 / M							0	0			
388 / M							0	0			
389 / M							0.5	0			
390 / M							0	0			
391 / M							0	0			
392 / M							0	0			
393 / M							0	0			
394 / M							0	0			

²Hours after induction dose.

¹Animals with scores greater than equal to or greater than 0.5.
²Sum of the erythema scores divided by the number of animals evaluated.